International Journal of Mycobacteriology 5 (2016) 354–356

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/IJMYCO

Case Report

Two cases of sternal osteomyelitis due to *Mycobacterium africanum*: a casual or causal association

Jessica Mencarini [a], *Sara Veloci* [a], *Maria Tullia Simonetti* [b], *Antonio Carocci* [c], *Massimo Meli* [c], *Enrico Tortoli* [d], *Gian Maria Rossolini* [b,e,f], *Alessandro Bartoloni* [a,c], *Filippo Bartalesi* [c,*]

[a] *Infectious Diseases Unit, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy*
[b] *Tuscany Regional Reference Centre for Mycobacteria, Microbiology and Virology Unit, Careggi Hospital, Florence, Italy*
[c] *Infectious and Tropical Diseases Unit, Careggi Hospital, Florence, Italy*
[d] *Emerging Bacterial Pathogens Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy*
[e] *Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy*
[f] *Department of Medical Biotechnologies, University of Siena, Siena, Italy*

ARTICLE INFO

Article history:
Received 13 May 2016
Accepted 23 May 2016
Available online 20 June 2016

Keywords:
Bone
Migrant
Tuberculosis
West Africa

ABSTRACT

The sternal localization of bone and joint tuberculosis (TB) is rare, has an insidious clinical presentation, and usually affects young adults living in endemic areas. *Mycobacterium africanum* causes a relevant proportion of human TB in West Africa and in migrants from endemic countries. Here, we report two cases of sternal osteomyelitis due to *M. africanum* in migrants.

Case report 1

In June 2014, a 33-year-old man was admitted to the Infectious and Tropical Disease Unit of Careggi Hospital, Florence, Italy. He came from Senegal and had been living in Spain and Germany before moving to Italy in February 2014. He reported weight loss and sweats for approximately 1 month and, in the previous 7 days, fever (39 °C) and swelling of neck lymph nodes. Physical examination revealed a fluctuant mass over the body of the sternum. Markers of inflammation were increased: C-reactive protein (CRP), 92 mg/L; erythrocyte sedimentation rate (ERS), 38 mm/h; and plasma fibrinogen, 540 mg/dL. The QuantiFERON-TB Gold (QFT) (Qiagen, Hilden, Germany) test was strongly positive (4.19 UI/mL). An echography of the neck revealed colliquative lymph nodes, and a chest radiography showed an apical right-pulmonary lesion. Computed tomography (CT) of the neck, chest, and abdomen showed a hypodense lesion in the presternal region, extend-

* Corresponding author at: Infectious and Tropical Diseases Unit, Careggi Hospital, Largo Brambilla 3, 50134 Florence, Italy.
E-mail address: bartalesif@aou-careggi.toscana.it (F. Bartalesi).
Peer review under responsibility of Asian African Society for Mycobacteriology.
http://dx.doi.org/10.1016/j.ijmyco.2016.05.006

ing into soft tissue (diameter 44 mm × 20 mm; Fig. 1). Spinal CT showed involvement of the cervical, dorsal, and lumbar spine, with multiple paravertebral abscesses compatible with tubercular osteomyelitis. Needle aspiration of the sternal abscess was positive for acid-fast bacilli (AFB), and the polymerase chain reaction (PCR) assay for *Mycobacterium tuberculosis* complex scored positive. The patient started first-line antitubercular therapy. The culture grew *Mycobacterium africanum* after 2 weeks of incubation. Susceptibility testing showed isoniazid resistance, therefore, isoniazid was dismissed. The respiratory specimens were also positive for *M. africanum*. The therapy was stopped after 12 months, with complete regression of sternal swelling, fever, and sweats, and normal values of the inflammatory markers. Whole-genome sequencing (WGS) assigned the strain to the spoligotype *M. africanum* West Africa Type 2 (MAF2) and confirmed the resistance to isoniazid.

Case report 2

In January 2015, a 21-year-old man from Senegal, in Italy since August 2014, was hospitalized. The patient reported a sternal trauma in November 2014, followed by painful swelling. Blood exams revealed a CRP of 29 mg/L, an ERS of 35 mm/h, and a normal value of fibrinogen (448 mg/dL). The QFT test scored positive (3.06 UI/mL). In the Emergency Department, he received a chest CT scan showing an osteolytic lesion of the sternal body and a presternal abscess (Fig. 2). No other organ was involved. A needle aspiration was positive according to AFB microscopy and PCR for *M. tuberculosis* complex. He started antitubercular first-line therapy. The culture was also positive, growing *M. africanum* after 3 weeks, which turned out to be susceptible to first-line antitubercular drugs. The therapy was stopped after 12 months, with complete regression of sternal swelling and pain. This strain was also assigned by WGS to the clade MAF2, although in a phylogenetic position very distant from that of the strain involved in Case report 1.

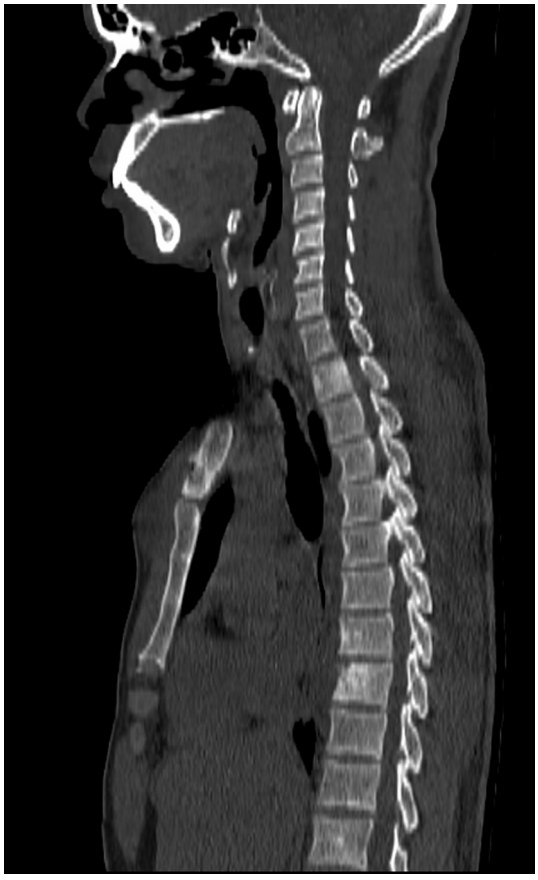

Fig. 1 – Computed tomography scan of the neck and chest, showing the presternal lesion extending into soft tissue.

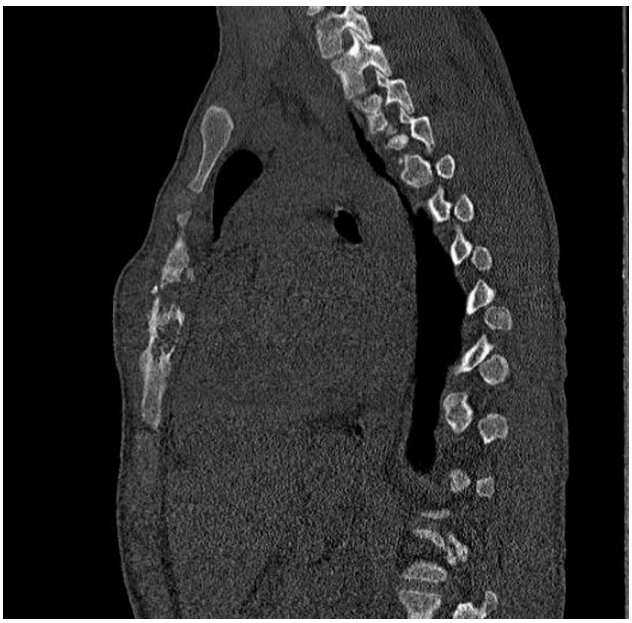

Fig. 2 – Computed tomography scan showing an osteomyelitis of the sternal body and a presternal abscess.

Discussion

In 2013, an estimated 9 million people developed tuberculosis (TB), with 6.1 million cases reported to the World Health Organization. Of these, 5.4 million were newly diagnosed cases, and among them, 800,000 were diagnosed with extrapulmonary TB (EP-TB) [1]. Although bone and joint TB is considered the third most frequent localization of EP-TB, involvement of the sternum is rare [2,3]. Its incidence ranges from 0% to 7%, has insidious clinical presentation, and is characterized by sternal pain and swelling [4]. Sternal TB can arise from either direct extension (hilar lymph nodes) or latent TB reactivation. Sternal TB usually affects young adults living in endemic areas and recognizes as risk factors open-heart surgery, human immunodeficiency virus (HIV) infection, intravenous-drug abuse, and Bacillus Calmette–Guérin vaccination [5]. Sternal radiography (Rx) can show bone loss, and CT more accurately characterizes soft-tissue involvement, but it is not superior to Rx in highlighting sternal involvement. Magnetic resonance (MR) images can show inflammatory changes in the medulla of the bone and allow discrimination between the reaction of the periosteum to the soft-tissue inflammation and osteomyelitis [6].

M. africanum was described for the first time in 1968 in Senegal and causes a sizeable proportion of human TB in West Africa [7]. Within the species *M. africanum*, two spoligotypes are present: (MAF1) prevalent around the Gulf of Guinea, and MAF2, prevalent in more western African countries [8]. In industrialized countries, its isolation was related to immigration from endemic countries, but in some cases, its dissemination was possible to native-born people and to immigrants from other regions [9,10]. The geographic restriction of *M. africanum* could be due to its adaptation to particular human populations in that region [11]. In Ghana, an ethnic polymorphism was associated with protection against Euro–American *M. tuberculosis*, but not against *M. africanum* and *M. bovis*, and this polymorphism may have allowed the establishment of *M. africanum* in West Africa [12]. A study compared the host-immunological response of Gambian HIV-negative patients to *M. africanum* and *M. tuberculosis*: before treatment in *M. africanum* infected patients, higher levels of tumor necrosis factor-α-producing CD4 and CD8 T cells were detected along with lower levels of interleukin-2-producing T cells, and after treatment, higher levels of activated T cells were persistently observed compared with those observed in TB patients [13]. MAF2 patients and household contacts were less likely to produce interferon-γ in an early secreted antigenic target-ESAT-6/culture filtrate protein-CFP-10 ELISPOT assay, and pathogen-related factors could be responsible for the lower response [14].

The clinical manifestations of *M. africanum* are similar to those of *M. tuberculosis*. Multiple localizations were reported for EP-TB due to *M. africanum*; including disseminated, cutaneous, genitourinary, pleural, osteoarticular, and brain mass [8]. To the best of our knowledge, this is the first report of sternal osteomyelitis caused by *M. africanum*. Although no data are available concerning the bone tropism of *M. africanum*, in both our case reports, this rare species of *M. tuberculosis* complex determined sternal osteomyelitis, suggesting a possible sternal tropism of *M. africanum*. In Europe, the increase of immigration from West Africa may account for an increasing incidence of TB due to *M. africanum*, and knowledge of the epidemiology could be helpful for the diagnosis of rare TB clinical manifestations.

Ethical standards

All persons gave their informed consent prior to their inclusion in the present article.

Conflicts of interest

The authors declare that they have no conflicts of interest.

REFERENCES

[1] World Health Organization (WHO), Global Tuberculosis Report 2014, WHO, Geneva, 2014. Available from: http://www.who.int/tb/publications/globalreport/en/ (last access: December 2015).

[2] A. Sandgren, V. Hollo, M.J. van der Werf, Extrapulmonary tuberculosis in the European Union and European Economic Area, 2002 to 2011, Euro. Surveill. 18 (2013). pii: 20431.

[3] H.M. Peto, R.H. Pratt, T.A. Harrington, et al, Epidemiology of extrapulmonary tuberculosis in the United States, 1993–2006, Clin. Infect. Dis. 49 (2009) 1350–1357.

[4] D.G. McLellan, K.B. Philips, C.E. Corbett, et al, Sternal osteomyelitis caused by *Mycobacterium tuberculosis*: case report and review of the literature, Am. J. Med. Sci. 319 (2000) 250–254.

[5] D.M. de Carli, M.D. Severo, C.J. Haygert, et al, Sternal osteomyelitis caused by infection with *Mycobacterium tuberculosis*, J. Bras. Pneumol. 35 (2009) 709–712.

[6] C. Atasoy, P.S. Oztekin, N. Ozdemir, et al, CT and MRI in tuberculous sternal osteomyelitis: a case report, Clin. Imaging 26 (2002) 112–115.

[7] M. Castets, H. Boisvert, F. Grumbach, et al, Tuberculosis bacilli of the African type: preliminary note, Rev. Tuberc. Pneumol. 32 (1968) 179–184 (Article in French).

[8] B.C. de Jong, M. Antonio, S. Gagneux, *Mycobacterium africanum*—review of an important cause of human tuberculosis in West Africa, PLoS Negl. Trop. Dis. 4 (2010) e744.

[9] M.C. Isea-Pena, M.F. Brezmes-Valdivieso, M.C. Gonzalez-Velasco, et al, *Mycobacterium africanum*, an emerging disease in high-income countries?, Int J. Tuberc. Lung. Dis. 16 (2012) 1400–1404.

[10] E. Desmond, A.T. Ahmed, W.S. Probert, et al, *Mycobacterium africanum* cases, California, Emerg. Infect. Dis. 10 (2004) 921–923.

[11] A. Asante-Poku, D. Yeboah-Manu, I.D. Otchere, et al, *Mycobacterium africanum* is associated with patient ethnicity in Ghana, PLoS Negl. Trop. Dis. 9 (2015) e3370.

[12] C.D. Intemann, T. Thye, S. Niemann, et al, Autophagy gene variant IRGM -261T contributes to protection from tuberculosis caused by *Mycobacterium tuberculosis*, but not by *M. africanum* strains, PLoS Pathog. 5 (2009) e1000577.

[13] L.D. Tientcheu, J.S. Sutherland, B.C. de Jong, et al, Differences in T-cell responses between *Mycobacterium tuberculosis* and *Mycobacterium africanum*-infected patients, Eur. J. 44 (2014) 1387–1398.

[14] B.C. de Jong, P.C. Hill, R.H. Brookes, et al, *Mycobacterium africanum* elicits an attenuated T cell response to early secreted antigenic target, 6 kDa, in patients with tuberculosis and their household contacts, J. Infect. Dis. 193 (2006) 1279–1286.